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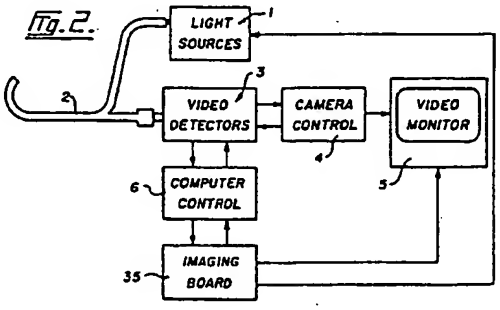
(54) Endoscopic imaging system for diseased tissue.

(57) Apparatus for imaging diseases in tissue comprising a light source for generating excitation light that includes wavelengths capable of generating characteristic autofluorescence for abnormal and normal tissue. A fibreoptic illuminating light guide is used to illuminate tissue with light that includes at least the excitation light thereby exciting the tissue to emit the characteristic autofluorescence. An imaging bundle collects emitted autofluorescence light from the tissue. The autofluorescence light is filtered into spectral bands in which the autofluorescence intensity for abnormal tissue is substantially different from normal tissue and the autofluorescence intensity for abnormal tissue is substantially similar to normal tissue. An optical system is used to intercept the filtered autofluorescence light to acquire at least two filtered emitted autofluorescence images of the tissue. The acquired images are displayed in real time on a display monitor in such a manner as to delineate abnormal and normal tissue.

Fig. 2.



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This invention relates to an apparatus for imaging abnormal tissues in the body to locate and identify areas that are otherwise not recognizable by white light endoscopy. The invention is particularly suited for imaging abnormal bronchial tissues to detect conditions such as inflammation, denudation, dysplasia and non-invasive early cancer (carcinoma in situ).

At present, the most effective method for examination of body cavities in human patients is by endoscopes. For examination of the air passages of the lung, a flexible endoscope is usually used, commonly referred to as a bronchoscope. Bronchoscopes, like all endoscopes, employs visible white light to illuminate the surface under examination. The illuminating light is brought into the air passages (bronchi) of the lungs via a fiberoptic illuminating light guide. The reflected and scattered light from the bronchial tissues is captured by a projection lens which focuses the image into the bronchoscope's imaging bundle. The imaging bundle is composed of several thousand individually wrapped fibers, which transmit a coherent image to the exterior of the body. This image is then projected through the ocular of the bronchoscope for human observation. A colour video camera can be attached to the eyepiece of the bronchoscope such that colour images of scattered/reflected white (broadband) light can be viewed on a colour video monitor.

Using a conventional bronchoscope, large invasive cancers can be readily seen. However, focal inflammation, denudation, dysplasia, and early lung cancers cannot be readily seen by such an apparatus.

Several methods have been developed to visualize small early lung cancers which are difficult to detect by ordinary white light bronchoscopy. All of these involve the use of tumour localizing drugs, e.g. Haematoporphyrin derivatives or Porfimer sodium, which have been shown to be preferentially retained in tumour tissues. Some of these drugs also fluoresce and their fluorescence can be detected by non-imaging and imaging devices (Profio AE et al., Med Phys 6:532-535, 1979; Profio AE et al., Med Phys 11:516-520, 1984; Profio AE et al., Med Phys 13:717-721, 1986; Hayata Y et al., Chest 82:10-14, 1982; Kato A, Cortese DA, Clin Chest Med 6:237-253, 1985; Montan S et al., Opt Letters 10:56-58, 1985). The drawback of these techniques is the use of drugs which may have serious side effects and therefore may not be appropriate for diagnostic purposes. In addition, the use of non-imaging devices such as the ratio fluorometer probe (Profio et al., Med. Phys 11:516-520, 1984) cannot delineate the exact site and dimensions of the abnormal areas.

An alternative approach for detecting invasive tumours has been proposed by Alfano et al in United States Patent 4,930,516 issued June 5, 1990. Alfano discloses a method of detecting cancers on the basis that the fluorescence spectra of cancerous tissues is different from normal tissues in that the maximal fluorescence peak of tumour tissues is blue shifted to lower wavelengths (from 531nm to 521nm). These observations were made based on in vitro measurements in excised, large (invasive) animal and human tumours but have not been reported on human tumours in vivo. In addition, there are no reports of other abnormal tissues such as inflamed or pre-cancerous tissues. We have measured tissue autofluorescence in human patients in vivo using different excitation wavelengths including 405nm, 442nm, and 488nm by a specially designed optical multichannel analyzer which can be attached to a conventional bronchoscope. Contrary to the observation by Alfano et al., we did not find any difference in the shape of the fluorescence spectrum between normal and tumour tissues using these excitation wavelengths. In particular, there was no blue shift of the emission peaks. We observed a significant difference in the overall fluorescence intensity especially in the green region of the visible spectrum. A significant but a lesser decrease in the overall fluorescence intensity was also found in pre-cancerous and non-cancerous lesions (dysplasia and metaplasia).

The decreased green fluorescence may be attributed to a reduced level of oxidized form of riboflavin. Riboflavin emits strongly in the green region and is believed to be predominantly responsible for the strong green fluorescence in normal human lung tissue. In the cancerous tissues, much less riboflavin was found (Pollack MA et al., Cancer Res 2:739-743, 1942) and/or is present in the reduced state. This may account for the reduced autofluorescence in pre-malignant and malignant bronchial tissues.

Tests were conducted revealing examples of such decreased tissue autofluorescence for dysplastic bronchial tissue, and carcinoma in situ. It was determined that the main difference between abnormal and normal tissues is manifested by a greatly reduced fluorescence intensity in the region of the spectrum from 480nm - 600nm. At wavelengths greater than approximately 635nm, the tissue autofluorescence is approximately the same between abnormal and normal tissues. Test were conducted using excitation light of 442nm, 405nm and 488nm and abnormal tissue results were compared to normal tissue results. All of these data were obtained in vivo during standard fiberoptic bronchoscopy using the optical multichannel analyzer.

Because of the observed large decrease in the emitted fluorescence without a change in the spectral profile in the abnormal tissues, methods using ratioing of two or more wavelengths that was originally described by Profio and coworkers and then studied in patients who have received fluorescent drugs such as Photofrin (Profio et al., Med. Phys. 11:516-520, 1984) generally will not differentiate abnormal from normal bronchial tissues using autofluorescence alone.

We have invented and constructed an apparatus

which exploits differences in autofluorescence intensity for the detection and delineation of the extent of abnormal areas in the human body, particularly the lung.

The present invention provides an imaging apparatus that uses autofluorescence characteristics of tissues to detect and delineate the extent of abnormal tissues in human patients in vivo. Capture and analysis of the autofluorescence images is achieved using a highly sensitive detector such as an image intensified CCD camera. A pseudo image is generated by sending one image to the red channel and one image to the green channel of an RGB video monitor. By capturing the two images simultaneously or sequentially within a few milliseconds, pseudo image generation in real time can be achieved. The pseudo images can clearly delineate the diseased tissue from the surrounding normal tissue.

Accordingly, the present invention provides an apparatus for imaging diseases in tissue comprising:

a light source for generating excitation light that includes wavelengths capable of generating characteristic autofluorescence for abnormal and normal tissues;

means for illuminating tissue with light that includes at least said excitation light thereby exciting the tissue to emit said characteristic autofluorescence;

collecting means for gathering emitted autofluorescence light from said tissue;

means for filtering said autofluorescence light into spectral bands in which said autofluorescence intensity for abnormal tissue is substantially different from normal tissue and said autofluorescence intensity for abnormal tissue is substantially similar to normal tissue;

optical means for intercepting said filtered autofluorescence light to acquire at least two filtered emitted autofluorescence images of the tissue; and

display means for displaying said acquired images in such a manner as to delineate abnormal and normal tissue.

In a preferred embodiment, the apparatus of the present invention is used with a standard bronchoscope for imaging abnormal bronchial tissues.

Aspects of the present invention are illustrated, merely by way of example, in the accompanying drawings in which:

Figures 1a to 1d provide examples of autofluorescence spectrums at selected excitation wavelengths which indicate the difference between abnormal and normal tissue;

Figure 2 is a schematic diagram showing the apparatus of the present invention useful for imaging abnormal lung tissue;

Figure 3 shows details of the illumination module;

Figure 4a shows the filtering and optical means of the present invention in which a single sensitive detector is used to acquire fluorescence images sequentially;

Figure 4b shows alternative filtering and optical means in which fluorescence images are acquired simultaneously using two sensitive cameras;

Figure 4c shows a still further filtering and optical means in which a prism element is incorporated to allow two fluorescence images to be acquired simultaneously together with a reflected/scattered excitation light image.

Figure 1 shows examples of decreased tissue autofluorescence for dysplastic bronchial tissue and carcinoma in situ. The main difference between abnormal and normal tissues is manifested by a greatly reduced fluorescence intensity in the region of the spectrum from 480nm - 600nm. At wavelengths greater than approximately 635nm, the tissue autofluorescence is approximately the same between abnormal and normal tissues. For the results in Figure 1a and 1b, a 442nm Helium Cadmium laser light was used to excite the tissues. Figure la shows tissue autofluorescence spectra of normal and dysplastic tissues and Figure 1b shows a carcinoma in situ (CIS) lesion compared to the normal tissue of a different patient. Similar results were found when employing other excitation light, e.g. 405nm, Figure 1c and 488nm, Figure 1d. In both cases carcinoma in situ patients are compared to their normal lung tissue. All of these data were obtained in vivo during standard fiberoptic bronchoscopy using an optical multichannel analyzer.

The apparatus of the present invention is designed to exploit the difference in fluorescence intensity in different regions of the spectrum to identify and delineate abnormal tissue.

The apparatus of the present invention adapted for use in examining bronchial tissues of the lung in patients is schematically illustrated in Figure 2. As such, the apparatus is integrated with a conventional bronchoscope used for examining bronchial tissue of the lung.

There is a light source 1 for generating excitation light that includes wavelengths capable of generating characteristic autofluorescence spectra for abnormal and normal tissue. The light source 1 is shown in greater detail in Figure 3 and preferably includes a laser light source 7 capable of producing excitation light at a selected desirable wavelength. A white light source such as an incandescent Xenon light source 8 can be used for white light illumination when desired. The laser light source 7 is use to generate pseudo images derived from tissue autofluorescence while the white light source is used to generate colour images of reflected/scattered white light.

The light from each light source passes through synchronizing means that allow for alternate illumination of the tissue by the laser light and the white light source. In the embodiment illustrated in Figure 3, the

synchronizing means comprises blocking means in the form of electronically controlled shutters 9 and 13 associated with laser light source 7 and Xenon light source 8, respectively. When shutter 9 is open to allow laser light to pass, shutter 13 is closed to prevent passage of white light and vice versa. The light from the laser light source 7 passes through shutter 9 when open, a mirror with a pin hole 10, and a lens 11 which focuses the laser light onto means for illuminating the tissue with light comprising a conventional bronchoscope light guide 12. Light guide 12 conducts the excitation light to the tissue area under examination. The tissue, upon illumination with the laser light, emits its characteristic autofluorescence for abnormal and normal tissue. To generate regular white light illumination images, shutter 9 is closed and previously closed shutter 13 is opened to allow the light from Xenon light source 8 to pass through shutter 13. The white light is then filtered by a neutral density filter set 14, reflected by a mirror 15, and passes through a lens 16 which focuses the light onto bronchoscope light guide 12 after being reflected off mirror 10 and through lens 11. The neutral density filter set 14 is used to condition the light from the Xenon source such that it is of the appropriate intensity for the light sensors used in the apparatus. Thus the white light conducted to the tissue illuminates the tissue under examination. Light guide 12 ensures that the light is evenly dispersed over the area under examination.

In the present embodiment, the bronchoscope provides the collecting means to gather images in the form of the bronchoscope lens (not shown) which collects scattered and reflected light, or emitted autofluorescence light from within the lung for transmission out of the body by imaging bundle 2 of the bronchoscope. This collected light is transmitted to a focusing lens 21 of the bronchoscope ocular coupled to the imaging bundle.

From the ocular of the bronchoscope, the collected light enters the image acquisition module 3 which includes means for filtering the autofluorescence light and optical means for intercepting the filtered light. Various embodiments of image acquisition module 3 are possible.

Figure 4a illustrates an image acquisition module that includes filtering means and optical means that allow for acquisition of emitted autofluorescence images sequentially. In this embodiment, the means for filtering the autofluorescence light comprises a series of filters that are sequentially insertable into the path of the emitted autofluorescence light to generate a sequence of filtered autofluorescence images. Filter wheel 18 is provided and is rotatably mounted beneath the optical means of the image acquisition module. When laser excitation light 7 is used, it is necessary to filter the autofluorescence light generated into at least two spectral bands. In one spectral band, the autofluorescence intensity for abnormal tissue is substantially different from that of normal tissue and in the other spectral band, the autofluorescence intensity is substantially similar to that of normal tissue. For example, in accordance with the characteristic spectral bands indicated in Figures 1a to 1d for lung examination, filter wheel 18 would be fitted with two filters. For laser excitation light of 442nm or 405nm, a green filter of 500+-20nm and a red 630nm longpass filter would be used. The green filter would filter the autofluorescence light into a spectral band in which the autofluorescence intensity for abnormal tissue is substantially different from that of normal tissue while the red longpass filter would filter the light into a spectral band in which the autofluorescence intensity is substantially similar for abnormal and normal tissue. The two filters are mounted in filter wheel 18 such that each covers one half of the filter surface. By rotating filter wheel 18 at an appropriate speed, red and green filtered autofluorescence images can be captured sequentially by optical means in the form of a single highly sensitive detector 17 such as an image intensified CCD camera.

The foregoing image acquisition module also includes additional optical means for capturing reflected/scattered white light images when white light source 8 is providing illumination of the tissue. A movable mirror 20 is provided that is insertable into the path of the collected light transmitted by ocular lens 21. Mirror 20 is positionable to deflect white light into a colour video camera 22 for acquisition of white light images. Necessarily, the movement of mirror 20 is controlled such that the mirror deflects the collected light into video camera 22 only when white light source 8 is providing illumination. Using white light source 8, colour images can be generated on a colour monitor in the same way as in conventional bronchoscopy. When laser light source 7 is illuminating the tissue, mirror 20 is removed from the light pass to allow for filtering of the autofluorescence light and subsequent acquisition by detector 17.

Figure 4b illustrates an alternative arrangement of image acquisition module 3 in which the optical means comprises at least two photodetectors that acquire filtered autofluorescence images simultaneously. Each photodetector has associated filtering means. For simultaneous collection of autofluorescence images, filter wheel 18 of the embodiment of Figure 4a is replaced by beam splitting means in the form of a dichroic mirror 24 which allows the red light >600nm to pass but reflects the shorter wavelengths. In this case, additional filters 25 and 26 for exact selection of the desired autofluorescence light can be employed and the respective images are focused onto two independent sensitive photodetectors such as image intensified CCD cameras 17 and 23. In Figure 4, filter 25 is a red 630nm longpass filter to further filter red light passed by dichroic mirror into a spectral band in which autofluorescence intensity is substan-

tially similar for normal and abnormal tissue. Filter 26 is a green filter of 500+-20nm for filtering the autofluorescence light into a spectral band in which the autofluorescence intensity for abnormal tissue is substantially different from that of normal tissue. Images acquired by the image intensified CCD camera 17 and/or image intensified CCD camera 23 are fed into red and green input channels of an RGB colour monitor 5 (Figure 1).

As in the arrangement of Figure 4a, reflected/scattered white light images created by white light source 8 are captured by a colour camera 22 and are displayed directly onto the colour monitor for visualization of the examined site using an identical movable mirror 20 insertable into the light path whenever white light source 8 is providing illumination.

Figure 4c illustrates a further embodiment of an image acquisition module for use with the apparatus of the present invention. A prism element 27 is provided that simultaneously splits collected light into a plurality of directions. By alternating between laser light source 7 and white light source 8, it is possible to capture sequentially both autofluorescence images and white light images within a 33 millisecond cycle time, therefore allowing a view of white (broadband) light colour images and pseudo fluorescence images at the same time on display means.

A specially developed camera with three photodetectors 28, 29 and 30 is provided. The prism 27 splits the collected light into three images which are then captured by the three separate detectors. Photodetectors 28 and 29 comprise CCD imaging devices that are provided with associated image intensifiers 37 and 38 and photodetector 30 is a regular CCD imaging device. Each photodetector has its own filter 32, 33 and 34, respectively, as well as an x,y,z micropositioner 31. Filters 32 and 33 are the same as in the previous embodiments: a 500+-20nm green filter 33, and a 630nm long pass filter 33. CCD imaging device 30 has an associated broadband blue filter 34.

As best shown in Figure 2, associated camera control electronics 4 are such that they generate three image signals, a red signal produced by red filter 32 and intensified CCD imaging device 28, a green signal produced by green filter 11 and intensified CCD imaging device 29 , and a blue signal produced by blue filter 34 and non-intensified CCD imaging device 30.

In all of the above embodiments, one can employ a specially designed CCD imaging device instead of an image intensified detector. For example, particularly when a lesser spatial resolution is required, several pixels of a sensitive scientific CCD detector can be electronically combined into a single very large pixel which allows very low signals to be detected.

All or some of the image signals produced by the various image acquisition modules of the present invention may be displayed directly on colour monitor 5 or processed by image processing means prior to display. The apparatus of the present invention can switch between white (broadband) light illumination and laser illumination in one thirtieth of a second.

Under laser illumination, the image acquisitio module of Figure 4c can collect autofluorescence images of the tissue over two selected areas of the spectra and a blue scattered/reflected excitation light image all simultaneously. These images can be combined either visually or mathematically via image processing means to make distinguishable the various tissue types present in the image. With white light illumination, the apparatus can collect red, green and blue reflected/scattered light images so as to make possible a regular colour image of the tissues.

Furthermore, the colour image can be combined with the autofluorescence blue laser illuminated images to enhance the detection, localization, and delineation of the various tissues.

For different tissues and/or diseases, a different combination of filters is employed to enhance the differences between normal and diseased tissues based on the characteristic emitted autofluorescence light of the diseased tissue under study.

As shown in Figure 2, the present invention is preferably provided with image processing means in the form of an imaging board 35 associated with a computer 6 that controls and co-ordinates operation of the apparatus. Imaging board 35 allows images to be digitally captured if desired. Board 35 acts to digitize the filtered images provided by the image acquisition modules and enhance the digitized images by application of transformational algorithms to produce pseudo computed images in real time for display on video monitor 5. Alternatively, the digitized images can be stored in computer memory.

The pixel values in the digitized images can be used to calculate a value for each image pixel, using a mathematical transformation, so that all pixels covering the diseased tissue site are clearly different from those of the normal tissue. This process can be used to enhance the images, to enable the measurement of the degree of the disease, and make possible other applications and/or measurements.

Several mathematical algorithms have been developed that allow the creation of different computed pseudo images from the digitized emitted autofluorescence images and scattered/reflected light images, provided the autofluorescence images are captured over the spectral areas that are characteristic and appropriate for the specific tissue disease. Examples of appropriate mathematical algorithms that can be programmed and applied to the digitized images include hue, contrast and intensity functions, principle component decomposition algorithms, logarithm of differences, and subtraction algorithms, all of which delineate normal tissues from the diseased tissues.

One transformation which has been reported with

tumour localizing drugs (Profio, Med. Phys. 11:516-520, 1984) was found by us not to be useful for the imaging method; with the exception of large invasive cancers, it often fails to reveal the abnormal areas.

In a preferred embodiment of the present invention, digitization of images and image processing is not required. By employing colour monitor 5 and the human visual system, it is possible to depict differences between the normal and diseased site as differences in perceived colour.

When using the image acquisition module of Figure 4b having two sensitive CCD cameras, one camera feeds the Red channel and the other feeds the Green channel of the RGB colour monitor 5. The red tissue autofluorescence of the abnormal and normal bronchial tissues is approximately the same. The green tissue autofluorescence is dramatically decreased in the abnormal site compared to normal tissue. Therefore the abnormal site appears much less green and much more reddish and/or sandy colour compared to the surrounding normal tissue which looks bright green as green fluorescence is much more dominant than red fluorescence in normal tissue. This preferred embodiment allows visualization of the diseased sites in real time without any processing of the images and is therefore very inexpensive.

The same result can be achieved using the single CCD camera and filter wheel of the image acquisition module of Figure 4a. In this case, two sequential red and green fluorescence images must be electronically combined at video rates to be fed as red and green input signals for an RGB monitor.

Alternatively, two different spectral bands of tissue autofluorescence are acquired and interpreted as red and green signals for colour display on a colour monitor. This gives excellent pseudo images of inflamed tissue, dysplastic tissue and non-invasive cancer; clearly delineating these tissues from normal tissue. The decrease in diseased tissue autofluorescence, particularly in the green region, indicates the presence of the disease as well as the severity of the disease.

If tumour localizing drugs are used, the apparatus of the present invention can be used to visualize small and large tumours. For example, for drugs such as Photofrin (Porfimer sodium), the same filters can be used as the drug emits fluorescence at peak values of 630nm and 690nm. In this case all sites where the drug has localized will also be clearly delineated from the normal tissues.

Although the present invention has been described in some detail by way of example for purposes of clarity and understanding, it will be apparent that certain changes and modifications may be practised within the scope of the appended claims.

Claims

1. Apparatus for imaging diseases in tissue comprising:

   a light source for generating excitation light that includes wavelengths capable of generating characteristic autofluorescence for abnormal and normal tissue;

   means for illuminating tissue with light that includes at least said excitation light thereby exciting the tissue to emit said characteristics autofluorescence;

   collecting means for gathering emitted autofluorescence light from said tissue;

   means for filtering said autofluorescence light into spectral bands in which said autofluorescence intensity for abnormal tissue is substantially different from normal tissue and said autofluorescence intensity for abnormal tissue is substantially similar to normal tissue;

   optical means for intercepting said filtered autofluorescence light to acquire at least two filtered emitted autofluorescence images of the tissue; and

   display means for displaying said acquired images in such a manner as to delineate abnormal and normal tissue.

2. Apparatus as claimed in claim 1 in which said display means comprises a colour monitor and said optical means provides at least two images that are fed to said monitor as two different colour signals to create a display image in which abnormal and normal tissue are recognized and delineated by changes in perceived colour.

3. Apparatus as claimed in claim 1 in which said light source uses a laser light for generating required excitation light.

4. Apparatus as claimed in claim 1 in which said light source includes a white light source for generating white light images for collection, acquisition and display in combination with said autofluorescence images.

5. Apparatus as claimed in claim 4 including synchronizing means to alternate between illumination of the tissue by said laser light and said white light.

6. Apparatus as claimed in claim 5 in which said synchronizing means comprises blocking means associated with each light source that prevents illumination of the tissue by one of said light sources when illuminated by the other of said light sources.

7. Apparatus as claimed in claim 6 in which said blocking means comprises a shutter.

8. Apparatus as claimed in claim 1 in which said means for illuminating tissue is the optical light guide of a bronchoscope.

9. Apparatus as claimed in claim 1 in which said collecting means is the imaging bundle and associated focusing lens of a bronchoscope.

10. Apparatus as claimed in claim 1 in which said optical means is an imaging photodetector that acquires said filtered autofluorescence images sequentially, said filtering means comprising a series of filters that are sequentially insertable into the path of said emitted autofluorescence light to generate the sequence of filtered autofluorescence images.

11. Apparatus as claimed in claim 10 in which said photodetector is an image intensified CCD.

12. Apparatus as claimed in claim 10 including additional optical means for capturing white light images when said white light images are being generated comprising a movable mirror insertable into said collected light to deflect white light images into a colour video camera.

13. Apparatus as claimed in claim 1 in which said optical means comprises at least two imaging photodetectors that acquire filtered autofluorescence images simultaneously, each photodetector having an associated filtering means.

14. Apparatus as claimed in claim 13 including beam splitting means to direct said emitted autofluorescence images to each of said at least two photodetectors.

15. Apparatus as claimed in claim 14 in which said beam splitting means is a dichroic mirror.

16. Apparatus as claimed in claim 13 in which said photodetectors are image intensified CCD.

17. Apparatus as claimed in claim 13 including additional optical means for acquiring white light images when said white light images are being generated comprising a movable mirror insertable into the path of said collected light to deflect white light images into a colour video camera.

18. Apparatus as claimed in claim 1 in which said optical means comprises a prism element for simultaneously splitting said collected light into a plurality of directions with associated filtering means and photodetector means to capture said light in each of said directions.

19. Apparatus as claimed in claim 1 including image processing means comprising:

digitizing means to digitize the filtered emitted autofluorescence images; and

image enhancing means for enhancement of said digitized images by application of transformation algorithms to produce pseudo computed images in real time.

20. Apparatus as claimed in claim 19 including memory storage means for storing the digitized images.

21. Apparatus as claimed in claim 19 in which said image processing means comprises an image processing board in a computer.

22. Apparatus as claimed in claim 19 in which said memory storage means comprises computer memory.

Fig.1a.

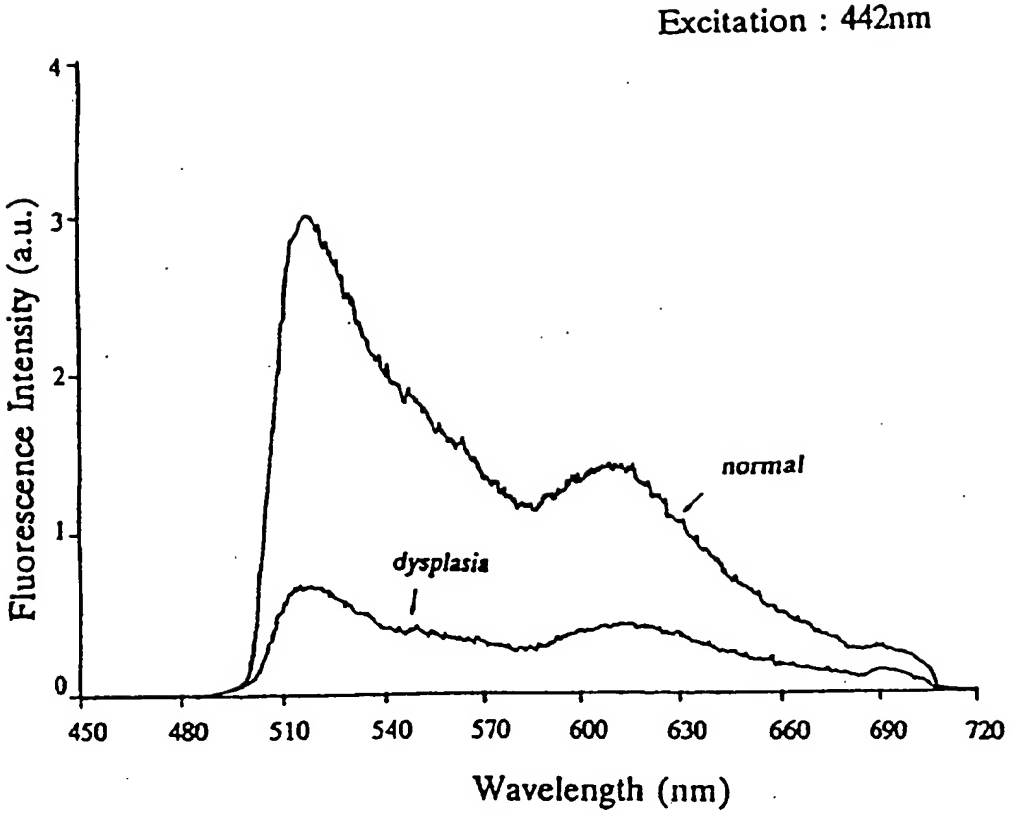

Excitation : 442nm
Fluorescence Intensity (a.u.)
0
1
2
3
4
450
480
510
540
570
600
630
660
690
720
Wavelength (nm)
normal
dysplasia

Fig. 1b.

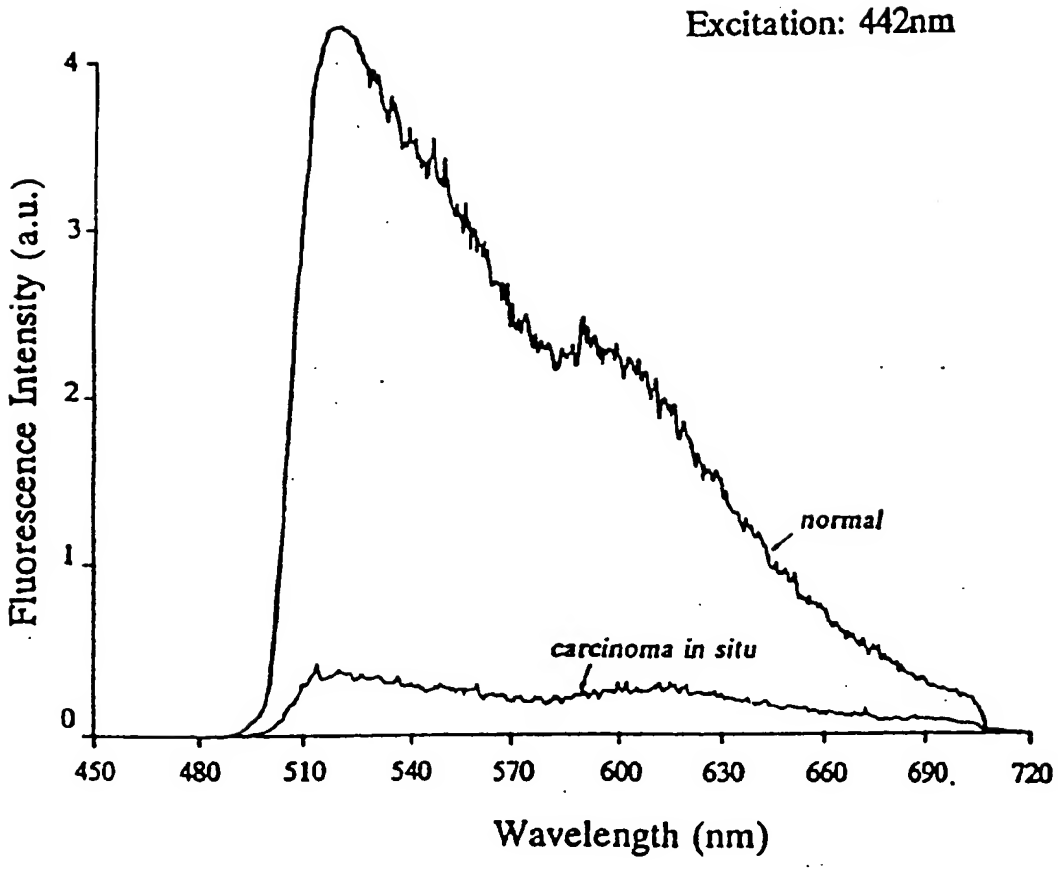
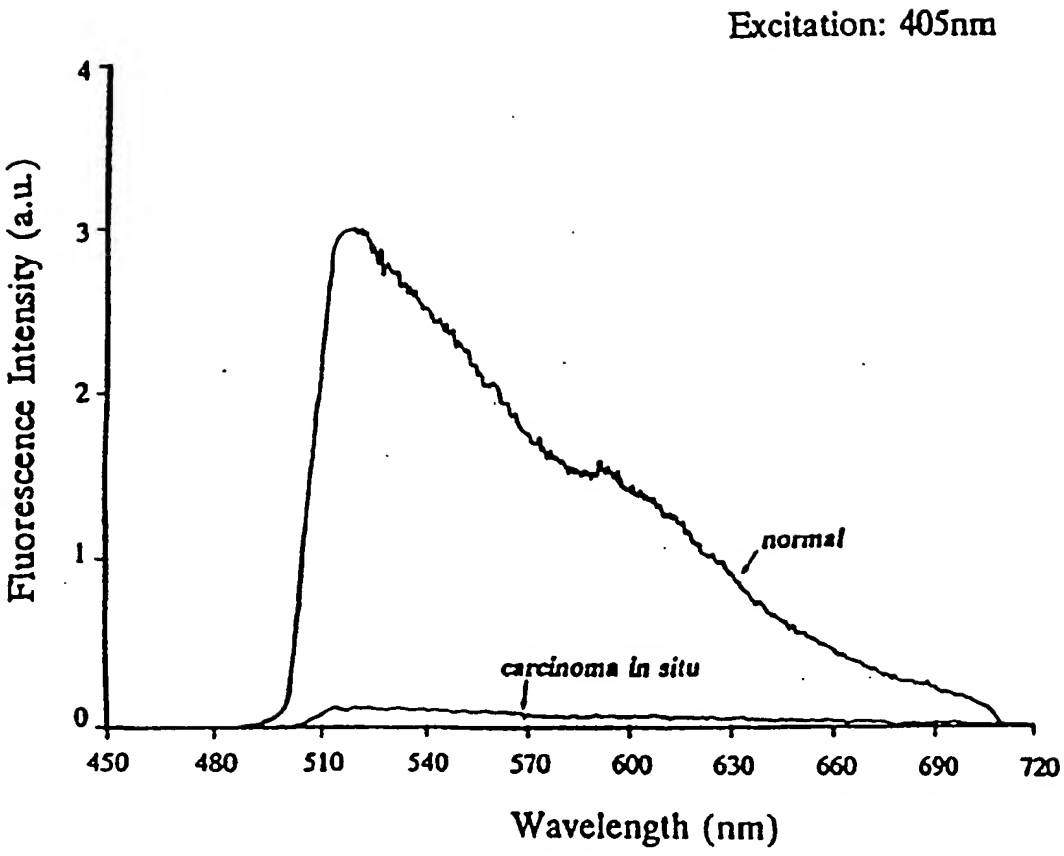

Excitation: 442nm
Fluorescence Intensity (a.u.)
0
1
2
3
4
450
480
510
540
570
600
630
660
690
720
Wavelength (nm)
normal
carcinoma in situ

Fig.1c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Fluorescence Intensity (a.u.)
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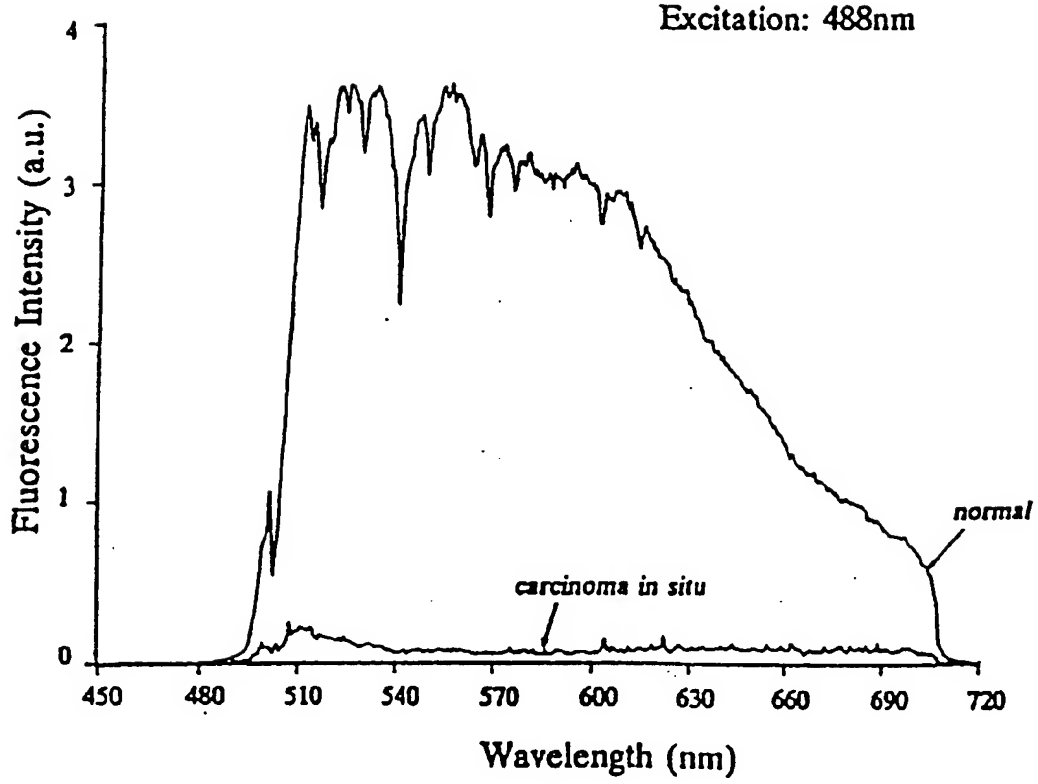
1
2
3
4
450
480
510
540
570
600
630
660
690
720
Wavelength (nm)
normal
carcinoma in situ

Fig.1d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2
3
4
450
480
510
540
570
600
630
660
690
720
Wavelength (nm)
normal
carcinoma in situ

Fig. 2.

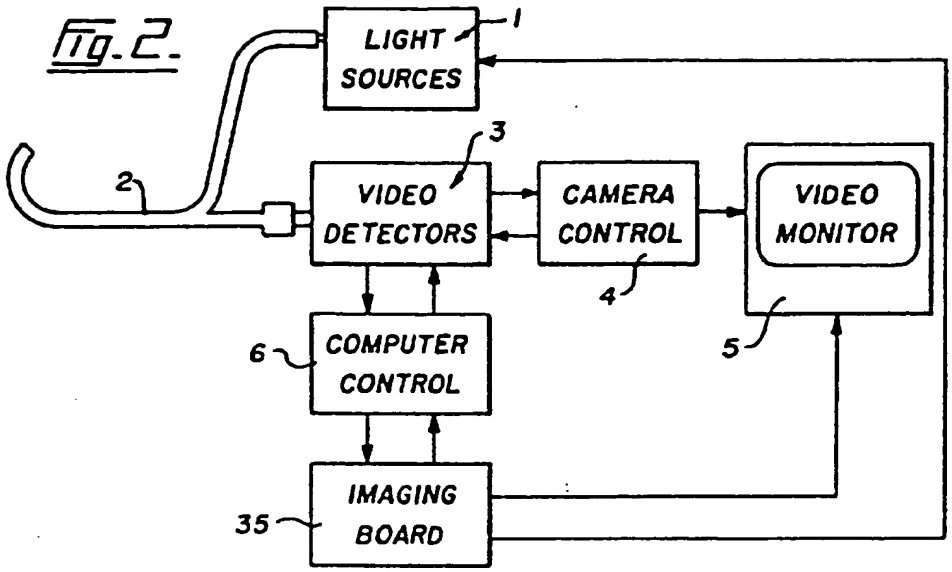

LIGHT SOURCES
1
2
3
VIDEO DETECTORS
CAMERA CONTROL
4
VIDEO MONITOR
5
6
COMPUTER CONTROL
35
IMAGING BOARD

Fig. 3.

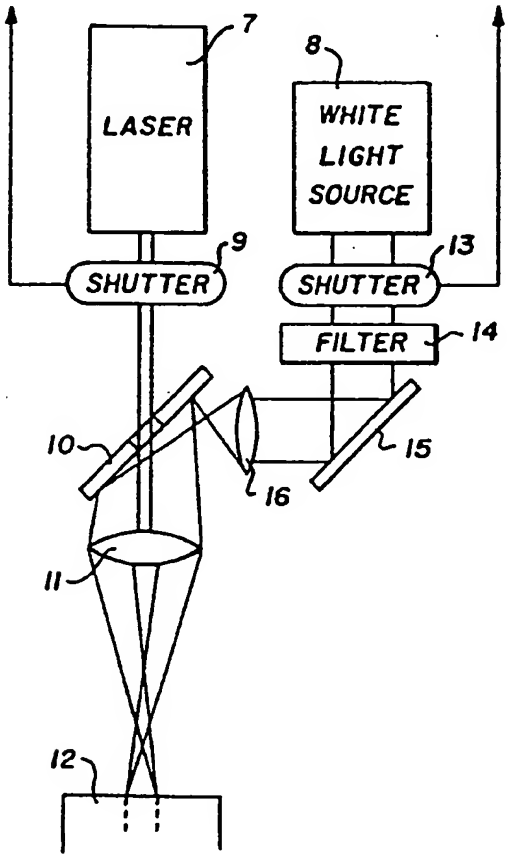

7
LASER
8
WHITE LIGHT SOURCE
9
SHUTTER
13
SHUTTER
FILTER
14
10
15
16
11
12

Fig. 4a.

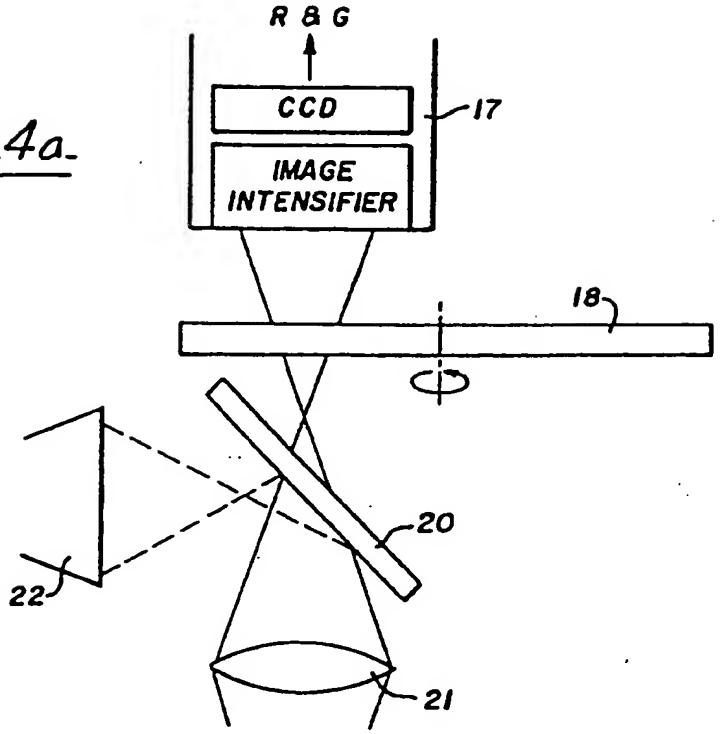

R & G
CCD
17
IMAGE INTENSIFIER
18
20
22
21

Fig. 4b.

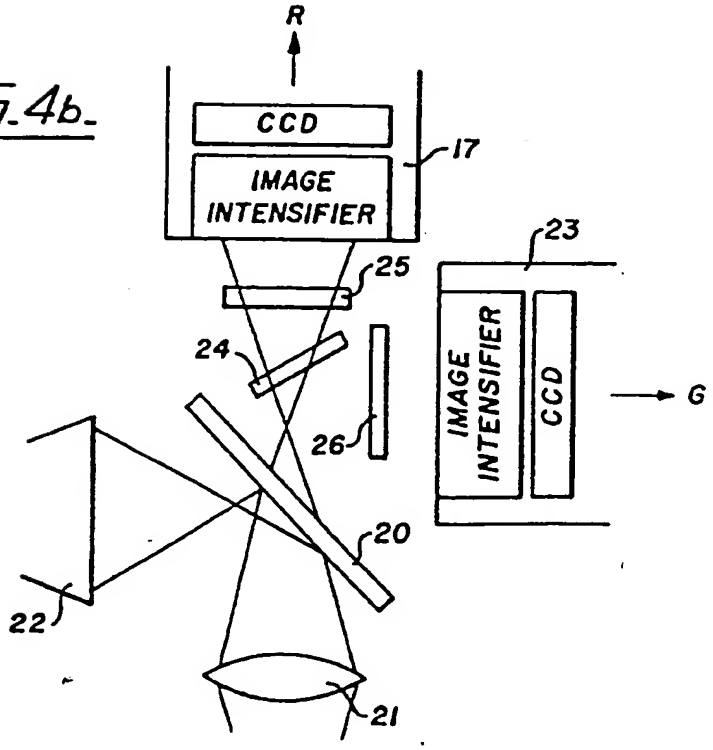
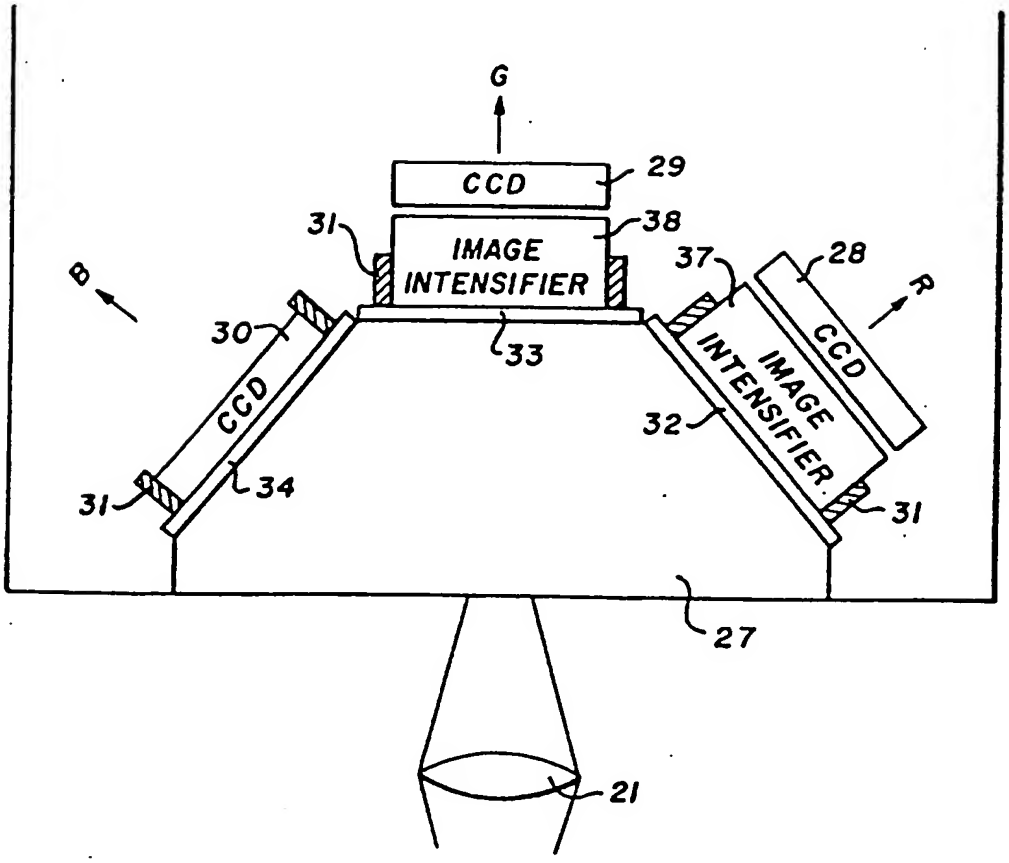

R
CCD
17
IMAGE INTENSIFIER
23
25
24
26
IMAGE INTENSIFIER
CCD
G
20
22
21

Fig. 4c.


G
CCD
29
31
IMAGE INTENSIFIER
38
37
28
R
B
30
33
CCD
IMAGE INTENSIFIER
CCD
32
31
34
31
27
21

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 92 85 0098

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	WO-A-9 010 219 (S.ANDERSSON-ENGELS ET AL.)	1,2,10, 11,13-16	A61B5/00
Y	* the whole document *	3-9, 18-22	
Y	US-A-4 718 417 (C.KITTRELL ET AL.) * the whole document *	3-7,18	
Y	US-A-5 003 977 (S.SUZUKI ET AL.)	19-22	
A	* the whole document *	12,17	
D,Y	MEDICAL PHYSICS. vol. 6, no. 6, November 1979, NEW YORK US pages 523 - 525; A.EDWARD PROFIO ET AL.: 'Laser fluorescence bronchoscope for localisation of occult lung tumors' * the whole document *	8,9	
X	WO-A-8 602 730 (HIGH-TECH NETWORK SCI AB) * the whole document *	1	TECHNICAL FIELDS SEARCHED (Int. Cl.5)
A	EP-A-0 215 772 (AVL AG) * page 14, line 20 - page 15, line 2; figure 8 *	13,14,16	A61B G01N
X	GB-A-2 203 831 (THE ACADEMY OF APPLIED SCIENCE INC.) * the whole document *	1	
X	WO-A-9 012 536 (MASSACHUSETTS INSTITUTE OF TECHNOLOGY) * page 11, line 1 - page 12, line 6; figure 1 *	1	

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	10 AUGUST 1992	HUNT B.W.

CATEGORY OF CITED DOCUMENTS

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